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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/081,739	02/21/2002	Walter Callen	09010-107001 / DIVER1530-	1077

45975 7590 12/21/2006

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EXAMINER	
RAO, MANJUNATH N	
ART UNIT	**PAPER NUMBER**
1652	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	12/21/2006	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	10/081,739	CALLEN ET AL.	
	Examiner	Art Unit	
	Manjunath N. Rao, Ph.D.	1652	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 August 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *See Continuation Sheet* is/are pending in the application.

4a) Of the above claim(s) *49-62,68-73,95-100,107,111-115,117-122 and 133-152* is/are withdrawn from consideration.

5)☒ Claim(s) *1,6,12,16,29,47 and 48* is/are allowed.

6)☒ Claim(s) *2,74,75,87,88,101-106 and 130-132* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims pending in the application are 1,2,6,12,16,29,47-62,68-75,87,88,95-107,111-115,117-122 and 130-152.

DETAILED ACTION

Claims 1-2, 6, 12, 16, 29, 47-62, 68-75, 87-88, 95-107, 111-115, 117-122, 130-152 are currently pending and are present for examination. Claims 1-2, 6, 12, 16, 29, 47-48, 74-75, 87-88, 101-106, 130-132 are now under consideration. Claims 49-62, 68-73, 95-100, 107, 111-115, 117-122, and 133-152 remain withdrawn from consideration as being drawn to non-elected invention.

Applicants' amendments and arguments filed on 8-7-06, have been fully considered and are deemed to be persuasive to overcome the rejections previously applied. Rejections and/or objections not reiterated from previous office actions are hereby withdrawn. Specifically Examiner has withdrawn the rejection under 35 USC 112, 2nd paragraph. Examiner has tentatively withdrawn the rejection of claims 74-75, 87-88, under 35 U.S.C. 102(b) as being anticipated by Imanaka et al. (GenBank Acc No. E13334, 4-28-1998) in view of the amendment. However, Examiner cautions applicants that said rejection will be reinstated if applicants fail to provide ample support for said amendment. Examiner acknowledges applicant's request to call them after review of the amended claims and remarks. However, Examiner regrets that he was unable to do so due to lack of time. With respect to applicant's request to rejoin claims drawn to method of making and using, Examiner will do so when all claims drawn to the products are in condition for allowance.

Election/Restrictions

Newly submitted claims 133-152 directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: These claims are drawn to

method of use of the polypeptide encoded by the polynucleotide of the elected group.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 133-152 have been withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 2, 74-88 and claims 101-106 and 130-132 depending therefrom are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 2 and 74 have been amended to recite the stringent hybridization conditions which comprises a hybridization in a buffer comprising 0.1X SSC, 0.5% SDS, 0.15 M NaCl for 15 minutes at about 72 degree C and a wash step. However, a perusal of the specification indicates that applicants have no support for said stringent hybridization using said buffer. Therefore claims 2, 74-88 are rejected for introducing "new matter" into the claims.

In response to the previous Office action, applicants argue that support for the amendment can be found in paragraph [0190] of the '634 Publication. However, a perusal of the

publication provides support for a buffer comprising only 0.1X SSC, and 0.5% SDS, and separately a buffer comprising only "0.15 M NaCl" but not for a buffer comprising both. Paragraph [0190] has been reproduced here for applicant's convenience. Examiner suggests deleting "0.15M" altogether.

> **[0190]** Following hybridization, the filter is washed to remove any non-specifically bound detectable probe. The stringency used to wash the filters can also be varied depending on the nature of the nucleic acids being hybridized, the length of the nucleic acids being hybridized, the degree of complementarity, the nucleotide sequence composition (e.g., GC v. AT content), and the nucleic acid type (e.g., RNA v. DNA). Examples of progressively higher stringency condition washes are as follows: 2×SSC, 0.1% SDS at room temperature for 15 minutes (low stringency); 0.1×SSC, 0.5% SDS at room temperature for 30 minutes to 1 hour (moderate stringency); 0.1×SSC, 0.5% SDS for 15 to 30 minutes at between the hybridization temperature and 68° C. (high stringency); and 0.15M NaCl for 15 minutes at 72° C. (very high stringency). A final low stringency wash can be conducted in 0.1×SSC at room temperature. The examples above are merely illustrative of one set of conditions that can be used to wash filters. One of skill in the art would know that there are numerous recipes for different stringency washes. Some other examples are given below.

It can also be seen that the above paragraph provides buffers for only the "washing" the membrane after hybridization but not for hybridization. Furthermore, Examiner reiterates that applicants have provided no support for the hybridization condition claimed because, the claim erroneously not only suggests using the "wash" buffers for hybridization but also indicates that there is wash step further. Therefore, Examiner suggests amending the claim accordingly by pointing to appropriate support in the specification or delete the claim altogether.

Claims 74-75, 87-88 depending therefrom are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains

subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claim 74 have been amended to recite the nucleic acid probes as that comprising "the nucleic acid has at least 97% identity over at least 75 or 100 consecutive nucleotides of SEQ ID NO: 1 or its fully complementary sequence; at least 95% identity over at least 150 and 200 consecutive nucleotides of SEQ ID NO: 1 or its fully complementary sequence; or, at least 90% identity over at least 300, 400, 500 or more consecutive nucleotides of SEQ ID NO: 1 or its fully complementary sequence". However, a perusal of the specification indicates that applicants have no support for said probes comprising said nucleic acid sequences. While Examiner found support for the fragments comprising 75, 100, 150, 200, 300, 400 or 500 consecutive nucleotides and found separate support for the percent identity language, he was unable to find support for the combination of fragments and percent identity language. Therefore claims 74-75, 87-88 are rejected for introducing "new matter" into the claims.

Claims 74-75, 87-88, are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a polynucleotide probe comprising or consisting of SEQ ID NO:1 encoding an enzyme having amylase activity and an amino acid sequence with SEQ ID NO:2, or a polynucleotide probe that is at least 95% identical to SEQ ID NO:1 encoding a polypeptide having amylase activity, and polynucleotides that are full length complement thereof does not reasonably provide enablement for any such polynucleotide probe wherein said probe hybridizes to amylase-encoding polynucleotide under highly stringent hybridization conditions

claimed in claim 74, or such probes comprising a detectable labels. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re Wands* (858 F.2d 731, 8 USPQ 2nd 1400 (Fed. Cir. 1988)) as follows: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claim(s).

Claims 74-75, 87-88, are so broad as to encompass any polynucleotide comprising a polynucleotide that is either a full length complement or partially complement to the polynucleotide of claims 1 or 2 or any polynucleotide (probe) that simple hybridizes to the polynucleotides of claims 1 or 2 under the stringent wash conditions at 72 degree C.
The scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of polynucleotides broadly encompassed by the claims. Since the amino acid sequence of a protein determines its structural and functional properties, predictability of which changes can be tolerated in a protein's amino acid sequence and obtain the desired activity requires a knowledge of and guidance with regard to which amino acids in the protein's sequence, if any, are tolerant of modification and which are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the proteins' structure relates to its function. However, in this case the disclosure is limited to the full-length nucleotide and encoded amino acid sequence of a single polynucleotide with SEQ D NO:1. It

would require undue experimentation of the skilled artisan to make and use the claimed polynucleotides and polypeptides. The specification is limited to teaching the use of SEQ ID NO: 1 as that encoding an amylase but provides no guidance with regard to the making of and using of complements, probes or with regard to other uses. In view of the great breadth of the claim, amount of experimentation required to make the claimed polypeptides, the lack of guidance, working examples, and unpredictability of the art in predicting function from a polypeptide primary structure (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-495), the claimed invention would require undue experimentation. As such, the specification fails to teach one of ordinary skill how to make and use the full scope of the polypeptides encompassed by this claim.

While enzyme isolation techniques, recombinant and mutagenesis techniques are known, and it is routine in the art to screen for multiple substitutions or multiple modifications as encompassed by the instant claims, the specific amino acid positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions. Therefore claims directed to nucleic acid probes comprising oligonucleotides as claimed in claim 74 can hybridize to any polynucleotide encoding alpha amylase i.e., a variant or mutant of SEQ ID NO:1 irrespective of whether the polynucleotide comprising the same encodes a polypeptide with SEQ ID NO:2. The specification does not

teach as to how those skilled in the art can use the same to detect a polynucleotide with SEQ ID NO:1 or a polynucleotide encoding a polypeptide with SEQ ID NO:2.

The specification does not support the broad scope of the claims which encompass all modifications and fragments of any polynucleotide encoding an amylase with sequence identity as described above because the specification does not establish: (A) a rational and predictable scheme for using all types of complements of SEQ ID NO:1; (B) a rational and predictable scheme for making and using all types of probes of SEQ ID NO:1to specifically detect SEQ ID NO:1; and (C) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Thus, applicants have not provided sufficient guidance to enable one of ordinary skill in the art to make and use the claimed invention in a manner reasonably correlated with the scope of the claims broadly including polynucleotides having no specific function. The scope of the claims must bear a reasonable correlation with the scope of enablement (*In re Fisher*, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, making and using of complements and probes having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See *In re Wands* 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

In response to the previous Office action, applicant has traversed the above rejection. Applicant argues, to address the scope, or breadth, of the claimed genus of nucleic acid probes, claim 74 has been amended to be expressly limited in scope to only encompass nucleic acids having at least 90% sequence identity to SEQ ID NO: 1 or its fully complementary sequence.

While applicants acknowledge that all species members of a genus of biological sequences must have a structure-function relationship, they aver that the linking functional limitation of the members of the genus does not necessarily have to be its natural biological function, but can be another function, e.g., as a research tool, for example, a probe to isolate or identify a protein-encoding sequence. Examiner respectfully disagrees. First of all it is not clear to the Examiner what applicants mean by saying that the claim has been amended to be expressly limited in scope to only encompass nucleic acids having at least 90% sequence identity to SEQ ID NO: 1. This is certainly not the case because the breadth of the claim has in fact been vastly enlarged by including probes as those nucleic acid sequence that are not only fragments of SEQ ID NO:1 but also sequences (fragments) that comprise a sequence that is at least 97% identical to any 75-100 nucleotides of SEQ ID NO:1 or 95% identical to any 150-200 nucleotides of SEQ ID NO:1 or 90% identical to 300, 400 or 500 or more consecutive nucleotides of SEQ ID NO:1. In some ways these claims are much broader than even claims 1 and 2. Furthermore, a probe of a claimed polynucleotide has to be specific for that polynucleotide. In the instant case the claimed polynucleotide probes includes those that are not only at least 95% identical to SEQ ID NO:1 and encoding a polypeptide with amylase activity but also probes that comprise fragments that have at least 97% identity over at least 75 or 100 consecutive nucleotides of SEQ ID NO: 1 or its fully complementary sequence; at least 95% identity over at least 150 and 200 consecutive nucleotides of SEQ ID NO: 1 or its fully complementary sequence; or, at least 90% identity over at least 300, 400, 500 or more consecutive nucleotides of SEQ ID NO: 1 or its fully complementary sequence. The genus of these probes are so large that using them to identify a polynucleotide comprising a sequence that is at least 95% identical to SEQ ID NO:1 and

encoding a polypeptide with amylase activity would constitute undue experimentation. Therefore, the above rejection is maintained.

Conclusion

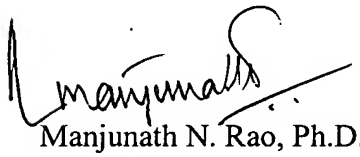
Claims 1, 6, 12, 29, 47-48 are allowable.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Manjunath N. Rao, Ph.D. whose telephone number is 571-272-0939. The Examiner can normally be reached on 7.00 a.m. to 3.30 p.m. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ponnathapura Achutamurthy can be reached on 571-272-0928. The fax phone numbers for the organization

where this application or proceeding is assigned is 703-872-9306/9307 for regular communications and for After Final communications. Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 571-272-1600.



Manjunath N. Rao, Ph.D.
Primary Examiner
Art Unit 1652

December 11, 2006